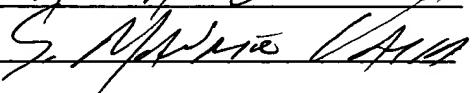


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PTO/SB/33 (07-05)

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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) PUJ-0279	
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		<p>First Named Inventor <u>Lorraine Elisabeth Pena</u></p>	
		Art Unit 1617	Examiner Shobha Kantamneni

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

I am the

applicant/inventor.
 assignee of record of the entire interest.
 See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed.
 (Form PTO/SB/96)

attorney or agent of record.
 Registration number 43,966

attorney or agent acting under 37 CFR 1.34.
 Registration number if acting under 37 CFR 1.34 _____



Signature

S. Maurice Valla

Typed or printed name

215-568-3100

Telephone number

March 23, 2006

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required.
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DOCKET NO.: PUJ-0279
Application No.: 09/634,399
Pre-Appeal Brief Request for Review

PATENT

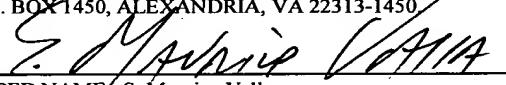
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Lorraine Elisabeth Pena, et al.
Application No.: **09/634,399**
Filing Date: **August 9, 2000**
For: **NOVEL COMPOSITIONS OF MINOXIDIL**

Confirmation No.: **5718**
Group Art Unit: **1617**
Examiner: **Shobha Kantamneni**

DATE OF DEPOSIT: March 23, 2006

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REGISTRATION NO.: 43,966

REMARKS TO SUPPORT PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants respectfully request review of the above-captioned application prior to filing of an appeal brief. Claims 1, 5 to 8, 10, 13 to 22, 30, 35, 62, 66, 68, 70 to 76, 111, 112, 115, 116 and 123 to 134 are pending, and stand rejected under 35 U.S.C. § 103(a).

The broadest claims are rejected over a combination of Preuilh, U.S. Patent No. 6,106,848 ("Preuilh") in view of Ewers, abstract of DE 19613698 ("Ewers") and Pena, U.S. Patent No. 5,225,189 ("Pena"). Additional references (Samour, U.S. Patent No. 5,620,980, and Sine, U.S. Patent NO. 6,423,329) are also relied on in combination with the foregoing references, as teaching specific elements of some of the dependent claims.

Applicants respectfully submit that the a proper *prima facie* case of obviousness has not been established by the Examiner. Moreover, to the extent that Preuilh, Ewers and Pena could have been initially combined to presumptively establish obviousness, the declarative evidence of record clearly establishes that the claimed subject matter is nonobvious.

The Subject Invention

The pending claims are all directed to *single-phase gels* (*i.e.*, not thickened or gelled two-phase emulsions), that comprise, *inter alia*, from about 5% to 8% minoxidil. The claims further require that the minoxidil be completely solubilized in a pharmaceutically acceptable solvent. Gelling is provided by inclusion of a *crosslinked copolymer of acrylic acid* as a thickening agent. Importantly, this requirement for a crosslinked copolymer of acrylic acid **does not** include carbomeric polymers, such as Carbopol® 910 and Carbopol® 934P, which the Preuilh and Pena references describe as useful gelling agents. Carbomeric polymers such as Carbopol® 910 and Carbopol® 934P are crosslinked *homopolymers* of acrylic acid, and are not suitable for use in the gels of the present invention, as shown in Example IV of the application.

Prima Facie Obviousness Has Not Been Established

1. Ewers is not a proper bridge between Preuilh and Pena.

The rejection relies on Ewers as motivation to combine Preuilh, which is solely directed to thickened *oil-in-water emulsions* with Pena, which teaches single-phase gels containing up to 3% minoxidil. Although Ewers does indicate that emulsion gels and single-phase gels may be used as alternative forms for transdermal delivery of a particular steroid hormone, the reference has nothing to do with minoxidil. The record clearly establishes that one of ordinary skill in the art of formulating minoxidil preparations would not be motivated to consult Ewers. *See* Pena Declaration, ¶ 11. Moreover, one of skill in the art would not conclude that the teaching in Ewers relating to transdermal administration of a steroid hormone would have any relevance or applicability to topical delivery of minoxidil, a completely unrelated (both chemically and therapeutically) compound. *See* Pena Declaration, ¶ 11; Pena Supplemental Declaration, ¶ 14.

Thus, the motivation that the Examiner asserts for combining Preuilh with Pena has been shown to be inconsistent with the understanding of those of ordinary skill in the art. Accordingly, Applicants respectfully assert that a *prima facie* case of obviousness has not been established.

2. Neither Preuilh nor Pena describe a single-phase gel containing from about 5% to about 8% minoxidil.

The Section 103(a) rejection relies on Preuilh as a teaching of stable compositions that contain the minoxidil concentrations recited in the claims. Preuilh is

broadly directed to oil-in-water emulsions that contain from “0.0001% to 20% by weight” of an active ingredient. Although minoxidil is included in a “laundry list” of possible actives, the patent further states that “the amount of the active agent in the composition according to the invention will depend on the active agent under consideration.” Thus, the reference does NOT teach that the compositions described therein may be prepared with up to 20% minoxidil, as the Examiner concludes, since the amount of active agent is said to vary, depending upon which of the vast number of actives is selected. Accordingly, Applicants respectfully submit that it is improper to rely on Preuilh as a clear teaching of gelled emulsions containing 5 to 8% minoxidil.

The Examiner asserts that “where the general conditions of a claim are disclosed in the prior art, discovering optimizing or workable parameters to obtain stable composition involves only routine skill in the art.” *See, e.g.*, Advisory Action dated March 2, 2006. However, Applicants have rebutted this assertion by submitting declarative evidence to establish that Preuilh cannot be relied on as a teaching of a gelled emulsion containing from about 5% to 8% minoxidil. The sole working example containing an active agent set forth in Preuilh is of an emulsion gel that contains 0.05% clobetasol propionate, a compound that is completely unrelated to minoxidil. The declarative evidence of record establishes that following this example with 3% minoxidil produces an unstable composition that separates into its composite phases. *See* Pena Declaration ¶ 16. Dr. Pena concludes from this experiment that even greater instability would result if the experiment were repeated with higher concentrations of minoxidil, such as from about 5% to 8%, as recited in the instant claims. *See* Pena Supplemental Declaration ¶ 11. The Examiner continues to ignore this evidence.

The Pena patent relied on by the Examiner fails to overcome the deficiencies of Preuilh. Pena describes single-phase minoxidil gels containing up to 3% minoxidil. The Examiner had previously attempted to assert that Pena described 5% minoxidil gels. However, Applicants established in the response submitted February 3, 2006, that this is not the case. The Examiner did not dispute this point in the Advisory Action.

Applicants respectfully assert that since neither Preuilh nor Pena describes or enables a single-phase gel containing from about 5% to about 8% minoxidil, a *prima facie* case of obviousness has not been established.

3. The Combined Teachings of Preuilh and Pena Would Not Lead One of Skill in the Art to Prepare a Single-Phase Gel Utilizing a Crosslinked Copolymer of Acrylic Acid as a Thickening Agent.

Preuilh is directed to *oil-in water emulsions*, not single-phase gels. Preuilh states that carbomers such as Carbopol® 910 and Carbopol® 934P are suitable for use as thickening or gelling agents. Pena teaches that Carbopol® 934P may be used to prepare single-phase gels containing up to 3% minoxidil.

Example IV of the instant application shows that carbomers such as Carbopol® 934P are not compatible with a 5% minoxidil gel of the present invention, however. Thus, even if Preuilh and Pena could be combined to suggest preparation of a single-phase gel containing from about 5% to about 8% minoxidil (which Applicants have shown they cannot), the combined teachings of these two references would lead one of ordinary skill in the art to utilize a thickening/gelling agent that has been shown to be unsuitable for use in the claimed invention.

Neither Preuilh nor Pena teaches that a crosslinked copolymer of acrylic acid, such as is recited in the instant claims, may be used as a thickening or gelling agent. Preuilh does indicate, however, that Pemulen® TR1 or TR1 may be used as an emulsifier, to emulsify the otherwise immiscible oil and water phases present in Preuilh's compositions. Applicants recognize that Pemulen® TR1 and TR1 are crosslinked copolymers of acrylic acid, as recited in the instant claims. Applicants respectfully assert, however, that one of ordinary skill in the art, if seeking to modify the oil-in-water emulsions taught by Preuilh by preparing a single-phase gel formulation, as taught by Pena, would not be motivated to include any emulsifying agent. Instead, Applicants submit that one of skill in the art would be motivated to select a carbomer, such as Carbopol® 934P, for use as a thickening or gelling agent, since that would be consistent with the teachings of both references.

The Examiner has failed to explain why one of ordinary skill in the art would include one of the emulsifying agents recited in Preuilh to make a single-phase gel in accordance with Pena. Pena neither teaches nor suggests that an emulsifying agent would be required or desired in a single-phase gel, and since there are not two phases to emulsify in a single-phase gel, one of ordinary skill in the art would have no reason to include such an ingredient. It is asserted in the Advisory Action that "Preuilh teaches that Pemulen TR1 is

compatible with minoxidil and results in stable compositions." However, Applicants respectfully submit that this fails to address the issue of why one of skill in the art would include an element that is taught as being suitable for an irrelevant purpose, or explain why the skilled artisan would reasonably expect that Pemulen TR1 could be used to thicken or gel a single-phase composition. Certainly, neither reference provides such a teaching.

Accordingly, Applicants respectfully submit that even if one were to conclude that Preuilh, Ewers and Pena may be properly combined to teach preparation of gel containing from about 5% to about 8% minoxidil, one of ordinary skill in the art would neither be motivated to utilize a crosslinked copolymer of acrylic acid as the thickening or gelling agent, nor reasonably expect that such a selection would be successful. Applicants respectfully submit, therefore, that a *prima facie* case of obviousness based on Preuilh in view of Ewers and Pena has not been established.

The remaining Section 103 rejections are all based on the combination of Preuilh, Ewers and Pena, in addition to other references (Samour and or Sine) that teach or suggest specific elements recited in certain dependent claims. Since these rejections all rely on the underlying rejection based on Preuilh, Ewers and Pena, Applicants respectfully submit that they also fail to establish the *prima facie* obviousness of any claims.

CONCLUSION

In view of the foregoing, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103, and allowance of all pending claims.

Date: March 23, 2006



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